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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,989	05/29/2001	Wilfred Wayne Lautt	2495.00071	7861

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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1614	

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12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/806,989	LAUTT, WILFRED WAYNE	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/16/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 1-3 and 19 are currently pending in this Office action and are the subject of the Office action.

Restriction/Election

Applicant's request for clarification of the restriction/election in the Office action mailed 5/16/07 at page 3, lines 10-19, is duly noted.

In response, the Office action mailed 5/16/07 is hereby amended to delete said restriction/election requirements as these requirements were inadvertently included in the action.

Response to applicant's arguments/remarks

Scope of enablement rejection under 112, 1st para (claims 1-3, and 19)

This rejection is withdrawn in view of applicant's amendment narrowing the scope of the invention.

Rejection under 103(a) (claims 1-3, and 19)

Applicant contends that this rejection should be withdrawn for the following reasons:

1) The cited references failed to establish a prima facie case of obviousness.

2) Adams et al. describe and claim methods of treating vascular tone to treat erectile and sexual dysfunctions (col. 1, lines 16-21; claims). There is no teaching or suggestion that the administration of No donors would affect endothelin in any other context besides vasoconstriction/vasodilation; and there is no teaching or suggestion that NO donors alone, or by mediating endothellin expression, would increase insulin sensitivity. It is in this context that Adams postulates that ET antagonists could be used for ... diabetes (col. 2, lines 24-31). The examiner has not provided a connection between NO donors and insulin sensitivity. That a prior art must be considered in its entirety, including portions that would lead away from the claimed invention, the Examiner has not provided predictable results to support a finding of obviousness.

3) Lautt et al. do not teach or suggest that parasympathetic neuropathy and insulin resistance is in any manner related to the actions of NO. The examiner has not provided a connection, or a motivation to explore, between NO donors and insulin responsiveness in view of Lautt et al.

4) The examiner is using hindsight reconstruction to combine known elements that do not have a reason to be combined.

In response, the rejection is maintained for the reasons made of record in the Office action mailed 10/16/07 at pages 10-12 and for the additional reasons set forth below:

a) It is the examiner's position that the cited references establish a prima facie case of obviousness as the prior art teaches the adminstration of known NO donor compounds. To the extent that the instant claims recite the step of administering specific known NO donors as the only active step, the contemplated effects to be achieved in practicing the instant claimed invention are considered to be coextensive with the administering of said compounds.

b) Lautt et al. teach that that insulin resistance is associated with liver disease and non-insulin dependent diabetes mellitus (NIDDM) and that patients with NIDDM may show insulin resistance, impaired glucose tolerance, and parasympathetic neuropathies (col. 1, lines 9-14).

c) Based on the teaching of Adams et al. that NO performs a function through interaction with endothelin (ET), and that ET is under inhibitory control of NO, such that administration of NOS inhibitors results in elevated levels of ET (column 2, lines 2-11), coupled with the disclosure that a number of investigators have postulated that ET antagonists could be used for conditions including diabetes (column 2, lines 24-31), someone of skill in the art would have been motivated to combine the cited art references to create the instant claimed inventive concept. Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, and 19 are rejected as being unpatentable over Adams et al. (US Patent 6,165,975; already made of record), in view of Lautt et al. (US Patent 5,561,165).

The above discussion of the rejection under 103(a) in connection with the Response to applicant's arguments/remarks is incorporated by reference.

Adams et al. teach a method of treatment, in an organism, of a vascular condition, comprising administration of at least one agent at a level which enhances NO and which does not appreciably alter normal systemic vascular tone in said organism. At least one agent is an NO donor selected from the group consisting of glyceryl trinitrate, isosorbide 5-ononitrate, isosorbide dinitrate, pentaerythritol tetranitrate, erythrityl tetranitrate, sodium nitroprusside, 3-morpholinosydnonimine molsidomine, S-nitroso-N-acetylpenicillamine, S-nitrosoglutathione, and N-hydroxy-L-arginine (see abstract). Instant claim 1 recites the following terms *"3-morpholinosydnonimine*

molsidomine (SIN-1)," *"nitroprusside,"* and *"S-nitroso-N-acetyl-D, L-penicillamine (SNAP)."* Adams et al. also teach that NO, in **humans and animals**, produced via sodium nitroprusside (SNP) infusion, causes vasodilation in peripheral vasculature at doses greater than 10 micrograms/kg per minute (column 1, line 66 to column 2, line 4); SNP may be administered in a convenient manner such as by injection (column 15, lines 35-37). Claim 1 also recites the term *"in a mammalian patient."* Claim 2 recites the term *"wherein said administering step comprises orally administering the compound,"* which is reasonably construed to overlap with the teaching of Adams et al. that SNP may be administered in a convenient manner (col. 15, lines 35-37). Claim 3 recites the term "wherein said administering step comprises injecting the compound," which also overlaps with the teaching of Adams et al. of SNP infusion (col. 15, lines 35-37). Adams et al. teach that NO performs a function through interaction with endothelin (ET), and that ET is under inhibitory control of NO, such that administration of NOS inhibitors results in elevated levels of ET (column 2, lines 2-11). Adams et al. also disclose that a number of investigators have postulated that ET antagonists could be used for conditions including diabetes (column 2, lines 24-31). To the extent that Adams et al. teach a method of treatment comprising administering NO donors such that No levels are enhanced (abstract), the NO compounds taught by Adams et al. are reasonably construed to satisfy the term *"administering to the patient an effective amount of a therapeutic nitric oxide donor compound"* as recited in claim 1 as these compounds are taught to enhance NO levels. The term "increasing insulin sensitivity" as recited in claim 1 is deemed to be coextensive with administering a therapeutic NO compound. Adams

et al. do not teach the limitation of hepatic sensitizing substance (HISS) dependent insulin sensitivity as recited in claim 19.

Lautt et al. (US Patent 5,561,165) teach a method for increasing insulin responsiveness and improving glucose tolerance in a mammal in which insulin responsiveness and glucose tolerance are impaired comprising administering an effective amount of a cholinergic agent (column 1, lines 35-40). Lautt et al. teach that non-insulin dependent diabetes mellitus (NIDDM) may show insulin resistance and impaired glucose tolerance, as well as parasympathetic neuropathies, and that patients with chronic liver disease also show insulin resistance (column 1, lines 9-14). The term *"wherein said insulin sensitivity is hepatic sensitizing substance (HISS) dependent insulin sensitivity"* as recited in claim 19 is reasonably construed to be coextensive with administering a therapeutic NO donor.

Based on the teaching of Lautt et al., someone of skill at the time the instant claimed invention was made would have been motivated to combine the teaching of Adams et al. and Lautt et al. to create a method for increasing insulin sensitivity in a diabetic patient comprising administering the NO donor compounds taught by Adams et al. Thus, someone of skill in the art at the time the instant invention was made would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Relevant Art of Record

The below art reference is made of record and relied upon is considered pertinent to applicant's invention.

Literati Nagy et al. (US Patent 6,887,872 B2) teach that only in fed state, nitrogen oxide causes the release of a hepatic insulin sensitizing factor (HISS) which possesses insulin synergent or insulin-like effect (column 19, lines 56-58).

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

19 December 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER